Technical Report No. 5

to the

Office of Naval Research
and
Advanced Research Projects Agency
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Contract Nonr 451(00)
NR 356-467

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Technical Report No. 5

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CHEMILUMINESCENT SYSTEMS

Monsanto Research Corporation
Boston Laboratory
Everett, Massachusetts 02149
Tel: 617-389-0480

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ABSTRACT

Maximum brightness and efficiency of the chemiluminescent autoxidation of indoles in basic solution in polar aprotic solvents is found for the 5- and 6-substituted skatoles. 2,3-Dimethylindole-5-carboxylic acid yields greater peak brightness than skatole at the standard 5×10^{-3}M concentration in DMSO, although with lower efficiency than skatole. The fluorescence spectrum of a basic solution of orthoacetamidoacetophenone, in DMSO, matches the chemiluminescence emission spectrum of 2,3-dimethylindole in peak wavelength and contour.

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I. INTRODUCTION

The objective of this research is the discovery of bright chemiluminescent reactions suitable for development into practical field systems. The previous reports in this series have outlined the results of a survey of the chemiluminescent autoxidative reactions of a number of different functional classes of organic compounds in basic solution in polar aprotic solvents.

In this report the major emphasis is on the chemiluminescence of substituted indoles. A survey has been made of the influence of substituents on the chemiluminescence parameters for commercially available compounds. A few structurally significant indoles have been synthesized. VPC analyses have been confined to determinations of related compound purities.

A principal result of this study has been the identification of some classes of substituents and substitutional positions which promote chemiluminescence brightness and efficiency in the autoxidation of indole and the identification of a group of indoles with chemiluminescence peak brightness or efficiency of the order of skatole. The compound 2,3-dimethylindole-5-carboxylic acid has been synthesized and has been found to possess greater peak emission brightness than skatole at the standard 5×10^{-3}M concentration.

For several of the better indoles, brightness and efficiency parameters have been obtained as a function of concentration and solvent. The chemiluminescence and fluorescence spectra have been determined for additional indoles and the fluorescence spectra of some possible reaction products have been determined. The fluorescence spectrum of one peak reaction product has been shown to match the chemiluminescence emission spectrum of 2,3-dimethylindole in peak wavelength and contour.

Preliminary experiments are reported on chemiluminescence spectral shifts observed in the oxidation of lucigenin adsorbed on silica.

II. CHEMILUMINESCENCE OF INDOLE DERIVATIVES

A. MONOSUBSTITUTED ALKYL INDOLES

To obtain a rational basis for the structural optimization of the chemiluminescence of the indoles, we have compared the gross peak brightness of the seven monomethyl compounds and of 3-ethylindole. The results obtained are summarized in Table 1. VPC analyses of the compounds were performed with emphasis upon determination of the skatole content. Corrections were applied for the skatole impurity assuming additivity of the peak brightness at the observed peak. Compared to indole, the 5- and 6-methyl compounds reveal large figures-of-merit (FM), about an order of magnitude below that of skatole. These large FM values are due largely, however, to long emission decay times rather than to high brightness. The skatole impurity content of 7-methylindole was not determined. Both the internal evidence (decay time and brightness) and the behavior of polysubstituted indoles (see following) lead us to suspect skatole contamination at the 0.3-0.5% level. Thus, again compared to indole, the 4- and 7-substitutions have only a very modest effect on the chemiluminescence. Both 1- and 2-substitution, on the other hand, depress the chemiluminescence markedly. The behavior of the N-methyl compound is, of course, of special interest since the very low brightness implies that the probable initial step in the oxidation is proton removal, in analogy to the luminol reaction (ref. 1).

It is clear from these results that the 3,5- and 3,6-dimethylindoles and 3,5,6-trimethylindole should be investigated. To obtain a standard skatole sample the commercial (EK) material was purified by zone refining (~70 zone passes). The apparent 50% increase in efficiency over the stock skatole is not considered to be significant at present since wide variations have been observed in previous comparisons made at long intervals (see concentration dependence section following).

B. INDOLES WITH OTHER SUBSTITUENTS IN THE BENZENE MOIETY

With the exception of 7-azaindole, all the compounds listed in Table 2 are 5- and 6-substituted. In large part, this reflects the availability of the materials. We have attempted to determine the chemiluminescence of 4- and 7-benzyloxyindole, but to date have found such extreme variability that the results are not interpretable.

The outstanding indoles in this group are the 5-cyano and 5-carboxyl and the 6-benzyloxy and 6-methoxy compounds, all of which are characterized by long decay half-lives rather than by high brightness. The 5-halogens show increasing efficiencies with decreasing electronegativity. 5-Bromoindole indeed possesses the long decay time of the more efficient members of this class but

Table 1

CHEMILUMINESCENCE OF MONOSUBSTITUTED ALKYL-INDOLES IN DMSO

Indole Concentration: 5×10^{-3}M
t-BuOK Concentration: $>5 \times 10^{-2}$M

Compound	Purity	% Skatole	100 I/I$_0$ Crude	100 I/I$_0$ Corrected[a]	t$_{1/2}$, seconds	Figure of Merit, seconds, Corrected[a] I/I$_0$ x t$_{1/2}$	Comments
Indole	99.7	0.3	30	5	250	13	Purified sample in preparation.
1-Methylindole	90.1	0.5	38	(≈0)	(450)	(≈0)	Major unidentified impurity ≈10%.
2-Methylindole*	100	0.0	6	6	54	3.2	High purity.
3-Methylindole	99.9	-	8.4×10^3	8.4×10^3	308	2.6×10^4	Averaged values: three impurity peaks.
3-Methylindole	99.98[b]	-	8.9×10^3	8.9×10^3	363	3.2×10^4	
4-Methylindole	89.4	0.0	1.3	1.3	(2.3×10^3)	30	No skatole, major unidentified impurity ≈10%.
5-Methylindole	100	0.0	30	30	3.3×10^3	10^5	High purity.
6-Methylindole	95.6	0.35	80 ± 30	50 ± 30	$(3.1 \pm 1.4) \times 10^3$	$(1.9 \pm 1.4) \times 10^5$	Average of six runs, highly variable, ten impurity peaks. Average of four runs for figure of merit.
7-Methylindole	99.0	?	40	40	360	140	Two unidentified peaks, skatole masked by major product.
3-Ethylindole	99.8	-	2×10^3	-	660	1.3×10^4	Comparable to skatole in brightness and efficiency.

* Previously reported.

a Peak brightness corrected for skatole impurity assuming molar additivity at observed peak.

b Zone refined sample.

Table 2

CHEMILUMINESCENCE OF INDOLES WITH SUBSTITUTED BENZENE MOIETY

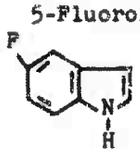
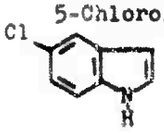
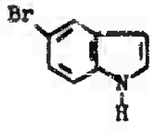
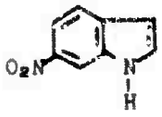
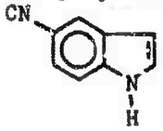
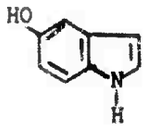
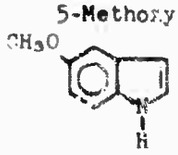
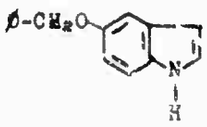
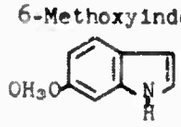
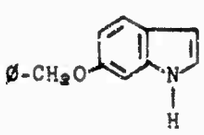
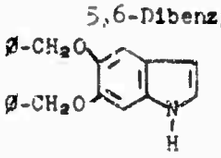
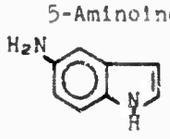
Compound and Structure	Peak O_2 Current I/I_0	Time to O_2 Peak sec	$T_{1/2}$ of O_2 Peak sec	Figure of Merit
5-Fluoroindole 	6×10^{-3}	70	200	1.2
5-Chloroindole 	$(2.6 \pm 1.0)10^{-2}$	53	720±60	18.7
5-Bromoindole 	$(1.7 \pm 0.3)10^{-2}$	255	6.4×10^{3}	88
6-Nitroindole 	2×10^{-4}	15	18	3.6×10^{-3}
7-Azaindole 	$(4.8 \pm 0.6)10^{-2}$	66	$(9.1 \pm 1.2)10^{3}$	4.4×10^{2}
5-Cyanoindole 	2.6×10^{-2}	-	3.2×10^{4}	8.4×10^{2}
5-Hydroxyindole 	2.6×10^{-3}	360	1.5×10^{3}	3.9

Table 2
(Continued)

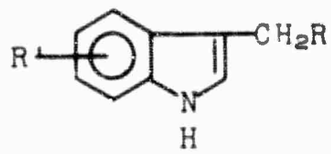
Compound and Structure	Peak O_2 Current I/I_0	Time to O_2 Peak sec	$T_{1/2}$ of O_2 Peak sec	Figure of Merit
5-Methoxyindole 	1.3×10^{-2}	-	120	1.6
5-Benzyloxyindole 	0.1	40	600	60
6-Methoxyindole 	0.5	-	$(6.4\pm1.4)10^{-3}$	$(3.2\pm0.8)10^{3}$
6-Benzyloxyindole 	0.75 ± 0.10	-	$(5.3\pm2.1)10^{3}$	$(4.4\pm1.4)10^{3}$
5,6-Dibenzyloxyindole 	0.38	40	1260	480
5-Aminoindole 	1.1	-	13	1.4

at much lower brightness. The 6-nitroindole compound is found to be the least efficient of the indoles, as may be expected from the known poor fluorescence efficiency of nitro-substituted compounds (ref. 2).

C. INDOLES WITH OTHER SUBSTITUENTS IN THE PYROLE MOIETY

Substitution at the 2-position of an indole derivative reduces the chemiluminescence efficiency markedly in all compounds investigated.*

A relatively large number of 3-substituted indoles, particularly skatole derivatives of structure,



have been investigated. The results are presented in Table 3 and are summarized in order of peak brightness in Table 4a and in order of figure-of-merit in Table 4B. The data generally support the conclusions derived from the monomethyl indole study.

Although quantitative analysis of substituent effects is not feasible, since most compounds of this group are of unknown purity, the qualitative effects are consistent for the brighter species. Thus, 5- and 6-substitution by methyl, methoxy and benzyloxy radicals increases the chemiluminescence efficiency of the indole-3 acetic acid, as does 5-carboxyl substitution. Similar effects are observed in tryptophan. On the other hand, 5-substitution of amino or hydroxyl groups leads to marked reduction in efficiency.

The effects of 3-substitution are both extremely marked and complex. Thus tryptophan is far less efficient than 3-ethyl indole, but indole-3-acetic acid is an order of magnitude more efficient than tryptophol.

The brightest indoles are all 3-substituted. Since 2-substitution reduces both efficiency and brightness, an obvious candidate for a brighter and more efficient indole is 3-methylindole-5-carboxylic acid. A thorough investigation of the 3,5,6-indoles as a class is clearly desirable.

A number of related heterocyclic compounds have been investigated with no outstanding candidates found. These results are given in Appendix I, together with the results for additional compounds included in the chemiluminescence survey.

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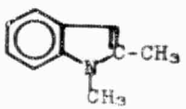
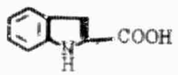
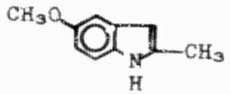
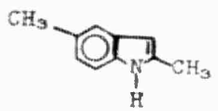
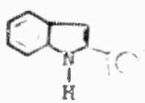
* A valid comparison cannot be made for the very weak N-methyl vs 1,2-dimethylindole, since impurity effects are clearly predominant.

Table 3

INDOLES WITH SUBSTITUENTS ON THE PYROLE MOIETY

Compound and Structure	Peak Brightness I/Io	Time to Peak Emission sec	$T_{1/2}$ sec	Figure of Merit	Comment[1]
		a) 2-Indoles			
1,2-Dimethyl indole 	1.2×10^{-2}		270	3.2	99.7%
Indole-2-carboxylic acid 	5×10^{-3}		300	1.5	
5-methoxy-2-methyl indole 	1×10^{-2}		360	3.6	
2,5-dimethyl indole 	0.89 ± 0.2	40	178 ± 28	15.7 ± 9	98.4%
2-phenyl indole 	2.4×10^{-3}	440	665	1.6	

1 Purities, where determined, are approximate mole-% as found by VPC analysis. The results for the substituted indole-3-acetic acids are based upon the observed distributions of decarboxylated products.

Table 3 (Cont'd)

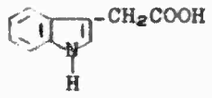
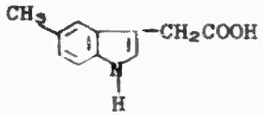
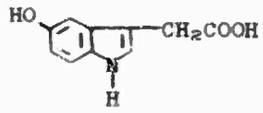
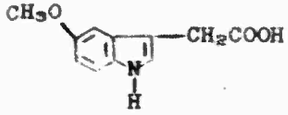
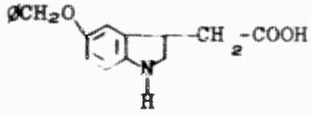
Compound and Structure	Peak Brightness I/Io	Time to Peak Emission sec	$T_{1/2}$ sec	Figure of Merit	Comment
		b) 3-indoles			
Indole 3-acetic acid 	9.1 ± 5.5	60	235 ± 15	2.1 x 10^3	
5-Methylindole-3-acetic acid 	24.6 ± 10.2	20	81 ± 21	(1.8 ± 0.3)10^3	85%
5-Hydroxyindole-3-acetic acid 	2 x 10^{-3}	48	240	0.5	
5-Methoxyindole-3-acetic acid 	45.2 ± 5.2	25 ± 3	99 ± 3	(4.5 ± 0.7)10^3	97%
5-Benzyloxyindole-3-acetic acid 	41 ± 5	42 ± 3	152 ± 28	(6.1 ± 0.4)10^3	97%

Table 3 (Cont'd)

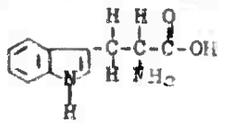
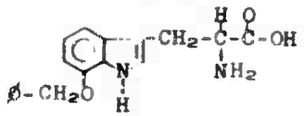
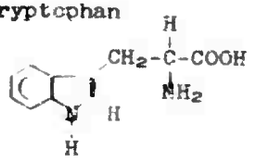
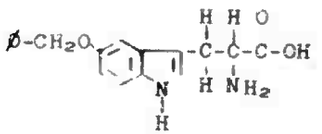
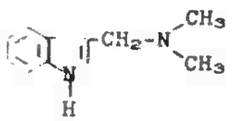
Compound and Structure	Peak Brightness I/Io	Time to Peak Emission sec	$T_{1/2}$ sec	Figure of Merit	Comment
5-Hydroxytryptophan 	$2.6(10)^{-3}$	30	180	0.47	
7-Benzyloxytryptophan 	$7(10)^{-2}$	30	900	63	saturated solution
L-Tryptophan 	.86	-	483	440	
Benzyloxytryptophan 	1.35 ± 0.05	60 ± 0	450 ± 60	605 ± 58	
Grammine 	0.11 ± 0.02	28	110 ± 70	12.1	

Table 3 (Cont'd)

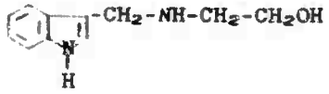
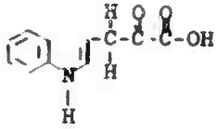
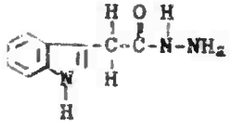
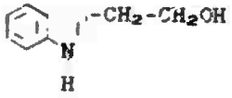
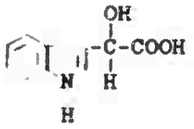
Compound and Structure	Peak Brightness I/Io	Time to Peak Emission sec	$T_{1/2}$ sec	Figure of Merit	Comment
(3-Indoylmethylamino)ethanol 	0.9×10^{-2}	20	48 ± 2.5	0.43	
Indole-3-pyruvic acid 	0.35 ± 0.06	15 ± 3	3.3 ± 0.3	1.15 ± 0.28	
Indole-3-acetic acid hydrazide 	1.18 ± 0.1	57	168 ± 12	197 ± 3	
Tryptophol 	0.76	70	450	342	
Indoleglycolic acid 	1.9×10^{-2}	36	276	5.2	

Table 3 (Cont'd)

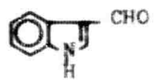
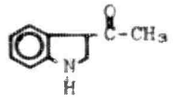
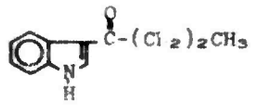
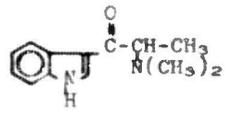
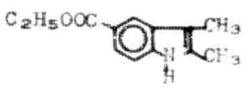
Compound and Structure	Peak Brightness I/I_0	Time to Peak Emission sec	$T_{1/2}$ sec	Figure of Merit	Comment
Indole-3-carboxaldehyde 	4.6×10^{-2}	60	300	13.8	
3-Acetylindole 	$(3.0 \pm 0.1)10^{-2}$	92 ± 12	321 ± 21	9.6	
3-Butyrylindole 	1.4×10^{-2}	12	48	0.67	
(β- Dimethylamino-propionyl)indole 	1.3 ± 0.3	65	600	7.8	
c) 2,3-Disubstituted Indoles					
Ethyl 2,3-dimethyl indole-5-carboxylate 	8	--	520	~160	100.0%

Table 3 (Cont'd)

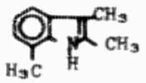
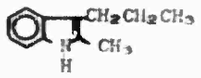
Compound and Structure	Peak Brightness I/I_0	Time to Peak Emission sec	$T_{1/2}$ sec	Figure of Merit	Comments
2,3-Dimethylindole-5-carboxylic acid 	156 ± 4	18 ± 3	48 ± 6	7540 ± 820	Solvents purged with N_2.
Same as above	111 ± 11	31 ± 11	42 ± 2	4710 ± 210	Solutions air saturated.
2,3,7-Trimethylindole 	14.4 ± 3.3	47	67 ± 9	965	97%
5-Amino-2,3-Dimethylindole 	4.3 ± 1.7	8	18 ± 4	68 ± 1.0	
2,3-Dimethyl-5-nitroindole 	not detected	--	--	--	
2-Methyl-3-propylindole 	6.7 ± 0.7	14	40 ± 2	266 ± 14	Crude product; ~50%

Table 3 (Cont'd)

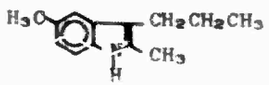
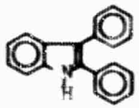
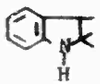
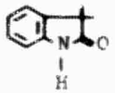
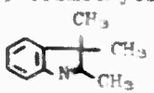
Compound and Structure	Peak Brightness I/I_0	Time to Peak Emission sec	$T_{1/2}$ sec	Figure of Merit	Comments
2,5-Dimethyl-3-propylindole 	17.2 ± 1.2	10	24 ± 0	413 ± 29	Crude product ~46%
2,3-Diphenylindole 	$2.1 \pm 0.7 / 10^{-3}$	≈10	≈15	3.2×10^{-2}	
d) Indole Derivatives					
Indoline 	0.4 ± 0.03	145	745 ± 35	298	
Oxindole 	0.19	20	1	--	
2,3,3-Trimethylindolenine 	0.83 ± 0.21	7 ± 2	27 ± 3	22 ± 4.5	

Table 4a

TABULATION OF BRIGHTER CHEMILUMINESCENT INDOLE DERIVATIVES -- IN ORDER OF PEAK GROSS BRIGHTNESS

	Compound	I/I_0
1.	2,3-Dimethylindole-5-carboxylic acid	134
2.	3-Methylindole	84
3.	2,3-Dimethylindole	60
4.	5-Methoxyindole-3-acetic acid	45
5.	5-Benzyloxyindole-3-acetic acid	41
6.	5-Methylindole-3-acetic acid	25
7.	3-Ethylindole	20
8.	2,5-Dimethyl-3-propyl, tech.	17*
9.	2,3,7-Trimethylindole	14
10	Indole-3-acetic acid	9

* Crude sample.

Table 4b

TABULATION OF BRIGHTER CHEMILUMINESCENT INDOLE DERIVATIVES -- IN ORDER OF FIGURE-OF-MERIT

	Compound	FM x 10^{-3}
1.	3-Methylindole	26
2.	3-Ethylindole	13
3.	2,3-Dimethylindole-5-carboxylic acid	6
4.	5-Benzyloxyindole-3-acetic acid	6
5.	5-Methoxyindole-3-acetic acid	4.5
6.	6-Benzyloxyindole*	4.4
7.	Ethyl-2,3-dimethylindole-5-carboxylate	4.2
8.	Indole-5-carboxylic acid*	3.8
9.	2,3-Dimethylindole	3.6
10.	6-Methoxyindole*	3.2

* Compounds with average emission decay times of the order of one hour. With the exception of indole-5-carboxylic acid, individual decay times are highly irreproducible.

III. INVESTIGATION OF INDOLE CHEMILUMINESCENCE

A. SOLVENT AND CONCENTRATION EFFECTS

We previously reported on the chemiluminescence peak brightness of skatole as a function of concentration in DMSO and DMF (ref. 3). These data have been extended and re-evaluated. The concentration dependence of the peak brightness is given in Figure 1 for skatole in the above solvents and in HPT (hexamethylphosphoric triamide), and for two additional indoles in DMF. These data are presented as the figure-of-merit/mole in Figure 2. This parameter is approximately related to the quantum efficiency of the reaction assuming that the emission spectrum and the order of reaction are constant, which is roughly true in the low concentration regions (see following sections). The optimum concentration for the brighter systems is clearly about 10^{-2}M.

The emission decay times have been observed to be highly irreproducible and apparently unpredictable functions of concentration for a given indole. For skatole in HPT we find the emission decay half-life to be a decreasing function of concentration; it is an increasing function in DMF and in DMSO a function with a maximum (Table 5). Both indole-3-acetic acid and 2,3-dimethylindole also show decay time maxima in DMF. However, since the observed maximum deviation of a single value is of the order of the total increment observed, we do not consider the results definitive. As may be seen from Table 5 the regular family of curves in Figure 2 in part reflects the relatively small increment in $t_{1/2}$ over the concentration range studied. Only for skatole in DMF is the maximum ratio as great as a factor of two.

As pointed out by Lee and Seliger (ref. 4), the observed rates of chemiluminescent reaction are subject to large variations presumably as a result of trace impurity catalysis, although the integrated emission, at least for luminol, is constant. We have attempted to incorporate a first order correction to this effect by use of the figure-of-merit, but propose in future photometry to measure the integrated emission directly. Greater precision could also be obtained by determination of the half-lives from kinetic analysis where simple rate law behavior is observed.

We have examined the chemiluminescence parameters of some representative indoles in HPT with the results given in Table 6. The very large variation observed in the figure-of-merit ratio between HPT and DMSO, for different indoles, although difficult to understand, suggests that further work in HPT is desirable to confirm and extend the above results.

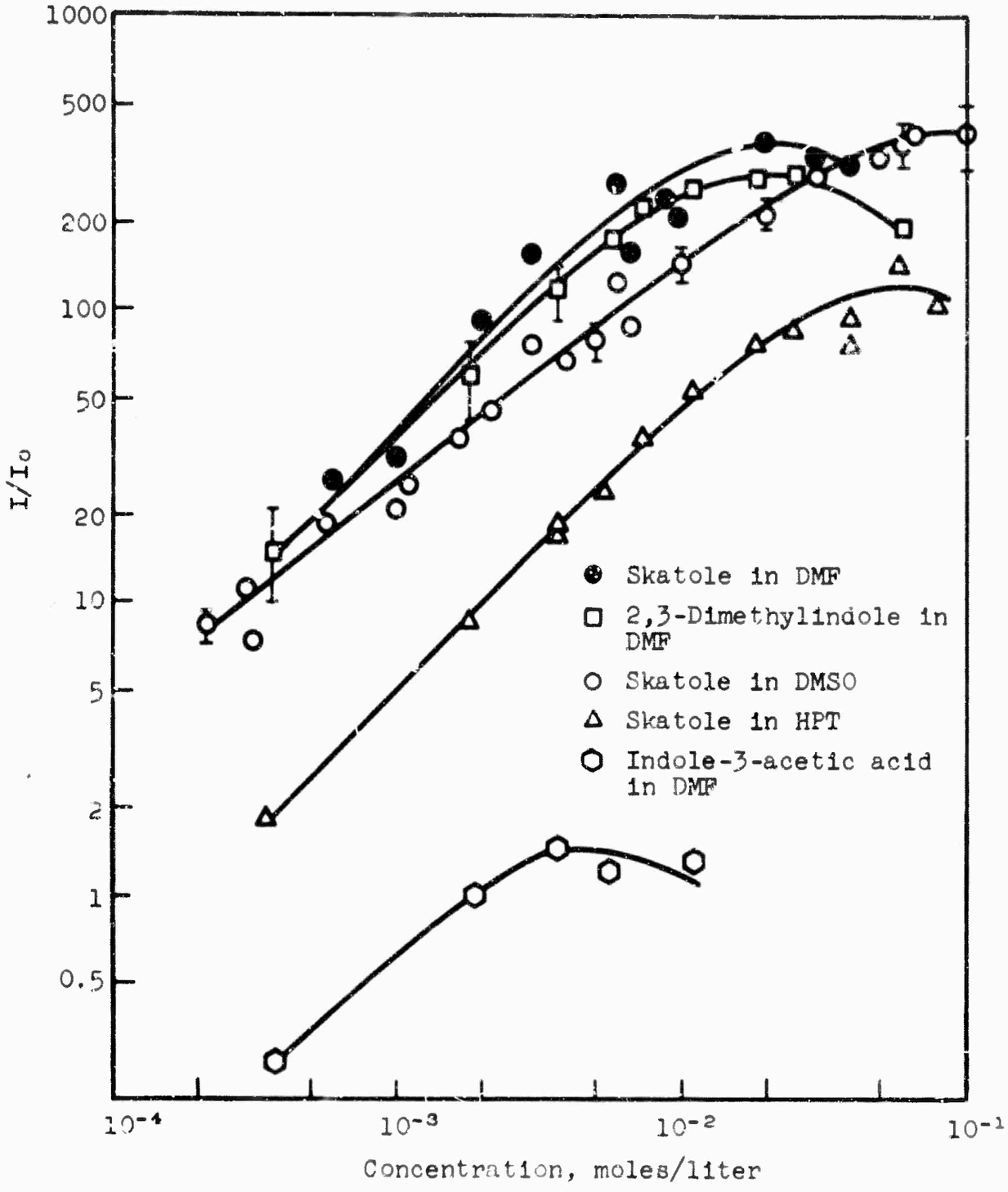


Figure 1. Concentration Dependence of Peak Brightness of Several Indoles

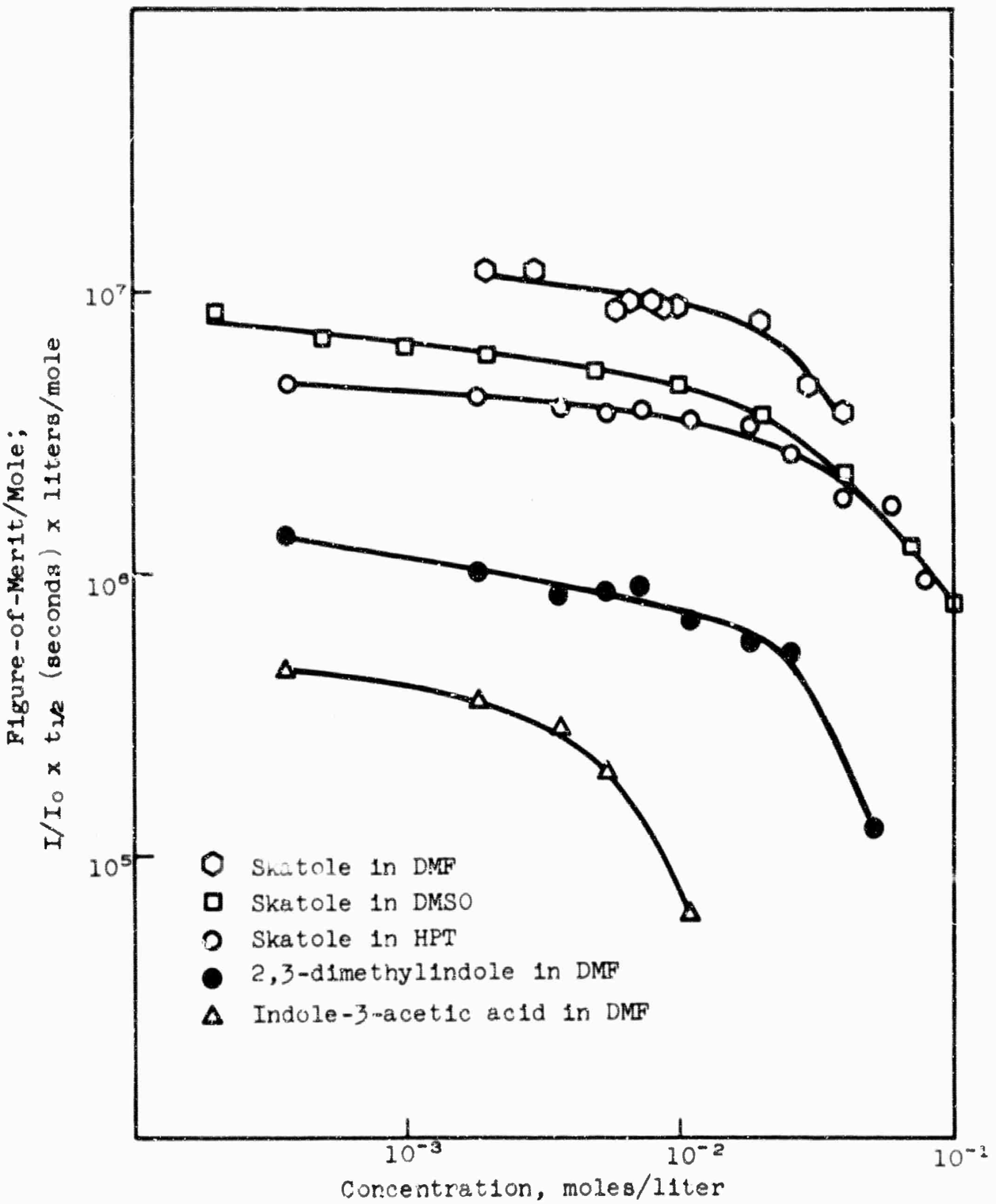


Figure 2. Concentration Dependence of Figure-of-Merit/mole for Several Indoles

Table 5

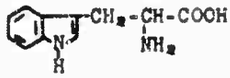
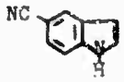
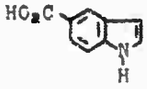
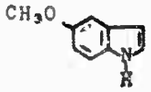
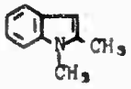
OBSERVED EMISSION DECAY INITIAL HALF-LIVES

Compound	Solvent	$t_{1/2}$ at Low Conc., seconds ≈5 x 10^{-4}M	$t_{1/2}$ at High Conc., seconds ≈7 x 10^{-2}M	$t_{1/2}$ Maximum Observed, seconds
Skatole	DMSO	240	200	235
Skatole	HPT	925	765	-
Skatole	DMF	240 (10^{-3}M)	450	-
2,3-Dimethylindole	DMF	30	35	40
Indole-3-acetic acid	DMF	640	540 (at 10^{-2}M)	900

Table 6

CHEMILUMINESCENCE PARAMETERS OF SOME INDOLES IN HPT SOLVENT

Indole Concentration: 5×10^{-3}M
Base Concentration: 0.1M

Compound and Structure	Peak O_2^- Current I/I_0	Time to O_2^- Peak, seconds	$t_{1/2}$ of O_2^- Peak, seconds	Figure-of-Merit, seconds	Figure-of-Merit in DMSO / Figure-of-Merit in HPT
Indole* 	2.2	42	60	132	0.1*
L-Tryptophan 	0.15	300	1440	216	0.5
5-Cyanoindole 	$(8.2 \pm 1.8)10^{-3}$	30 ± 30	430 ± 290	3.0 ± 1.6	$(2.8 \pm 1.5)10^{2}$
Indole-5-carboxylic Acid 	4.6×10^{-2}	48	180	8.3	2.1×10^{2}
Indole-2-carboxylic Acid 	8.4	40	40	336	4.5×10^{-3}
5-Methoxyindole 	6.4 ± 0.2	40 ± 10	39	245 ± 34	$(6.4 \pm 0.9)10^{-3}$
1,2-Dimethylindole 	8×10^{-4}	240	360	0.5	10

* Datum corrected for 0.1% skatole impurity; 99.7% pure by VPC analysis.

B. THE MECHANISM OF INDOLE OXIDATION

1. General Background

The identification of the light-emitting species in the indole chemiluminescence reaction would greatly aid attempts to optimize the system. A number of references relating to the oxidation of 2,3-disubstituted indoles have appeared in the literature during the past fifteen years. The work of Robertson (ref. 5-7) and Witkop (ref. 8 and 9) is especially pertinent.

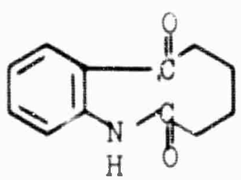
While none of the literature work relates to reactions in dimethylsulfoxide solution, the reaction products that were identified give clues to the types of reactions that might take place in our chemiluminescent system. A summary of this literature work is given below in Figure 3.

2. Discussion

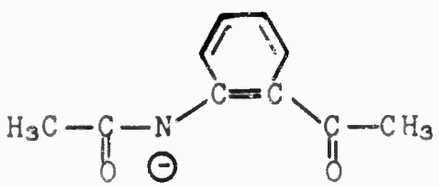
From data available in the literature, several compounds emerge as candidates for the chemiluminescent species in indole oxidation reactions.

The excited state of o-acetamidoacetophenone (H) must be considered as the prime candidate for the light emitting species in the 2,3-dimethylindole (F) oxidation reaction. The fluorescence emission of (H) in basic dimethylsulfoxide solution corresponds closely to the chemiluminescence emission of (F) (see Section III.C). This type of intermediate might explain the difference in light emission between compounds (A) and (F). While (F) forms a dicarbonyl derivative (K) which is analogous to (H), (K) reacts to produce compound (C) (ref. 7, 8); (H) apparently does not react further (ref. 7). In addition, the anion of (H), [compound (L)] has a structure that is very similar to (M), the anion which is postulated to be the emitting species in the lophine chemiluminescence reaction (ref. 10).

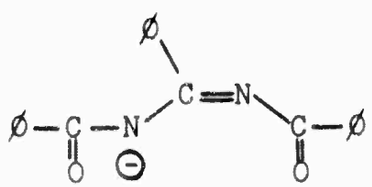
O-Formamidoacetophenone, the skatole intermediate analogous to (H), is currently being prepared as a further test for this type of intermediate.



(K)



(L)



(M)

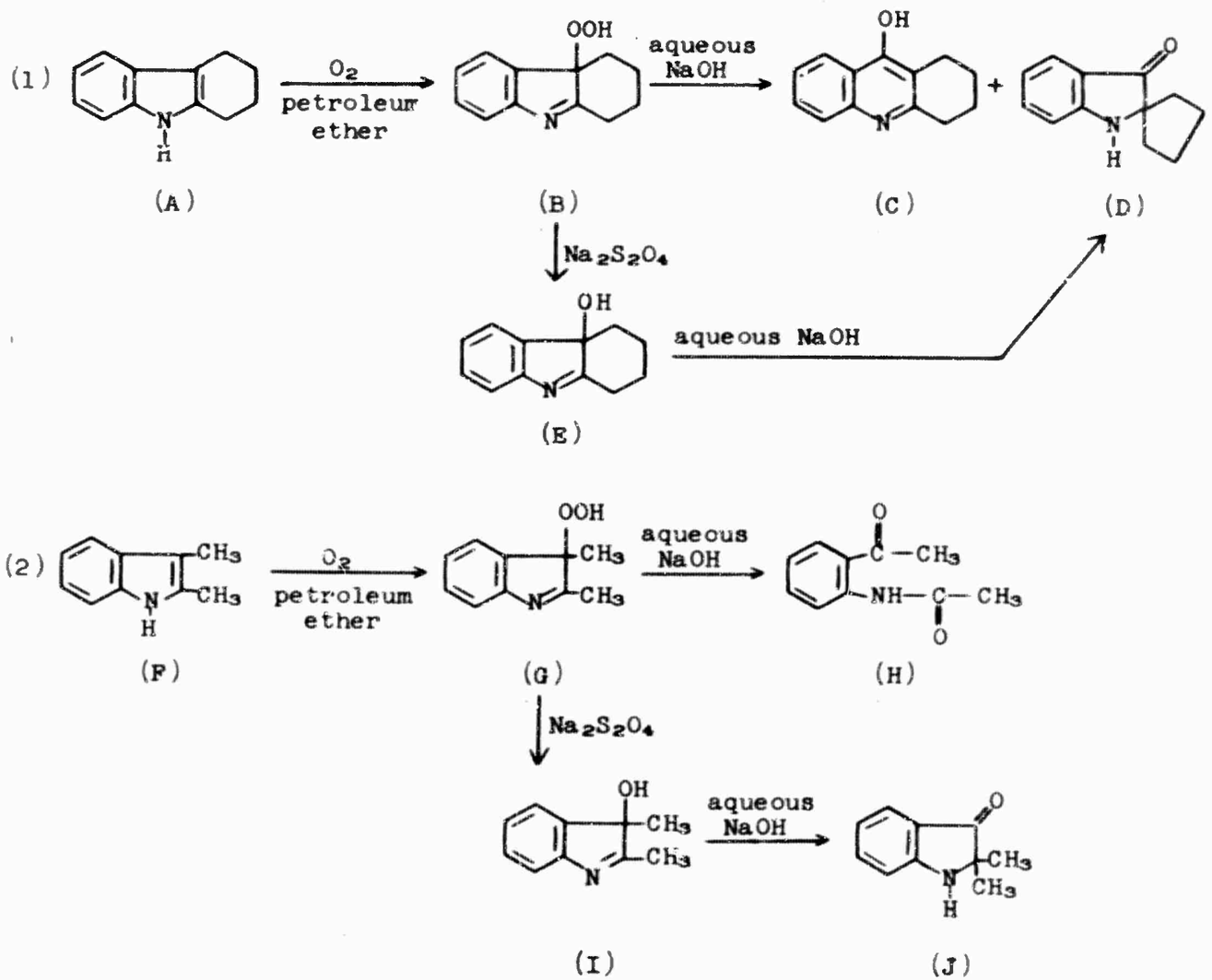


Figure 3. 2,3-Disubstituted Indole Oxidation Products

Tetrahydrocarbazolyl hydroperoxide (B) and its 5-carbomethoxy derivative give off flashes of blue and green light when thermally decomposed. This indicates that the energy available from peroxide decomposition is of the proper magnitude to be detected as visual chemiluminescence. The fact that tetrahydrocarbazole (A) is not chemiluminescent under our reaction conditions may be due to the facile formation of nonfluorescent products such as (C) in solution.

Finally, the 3-indoxyls (D and J) should be considered as possible chemiluminescent intermediates. This type of compound is known to be formed from 2,3-disubstituted indoles under basic autoxidation conditions. These compounds are noted for their intense green fluorescence in solution (ref. 5-7). Since the indoles chemiluminesce in the green region of the visible spectrum, the excited state of (J) is a possibility for the chemiluminescent species in the oxidation of 2,3-dimethylindole (F).

While it is tempting to postulate detailed reaction mechanisms to explain the observed substituent effects, we feel that this speculation should be deferred until most of the proposed intermediates are examined experimentally. Compounds G, I, and J are currently being synthesized to test the above mentioned hypotheses.

C. CHEMILUMINESCENCE AND FLUORESCENCE SPECTRA OF THE INDOLES

The indoles for which chemiluminescence spectra have been determined are given in Table 7. The emission spectra peak in the green at about 500 nm. The fluorescence peak wavelengths of the parent indoles are in the near ultraviolet at about 350 nm. Addition of base produces a rather large shift to the red of the order of 50 nm (with the exception of 7-methylindole). In all examples the resulting anion fluorescence peak is 50-100 nm below the chemiluminescence peak wavelength.

The fluorescence spectra of oxidized solutions of skatole and 2,3-dimethylindole (ref. 3) possess emission bands which correspond to the chemiluminescence emission spectra in shape and peak wavelength (Figure 4) indicating that for these compounds the emittor species is reasonably stable to further oxidation. The uncorrected fluorescence spectrum of base-free skatole in DMSO peaks at 356 with a shoulder at 370 nm. The corrected spectrum (relative photons/cm^{-1}) peaks at 350 nm and eliminates the shoulder. During the course of the oxidation of skatole, the anion fluorescence at ca. 420 nm is observed to diminish in intensity, and the intensity at ca. 490 nm increases.

The overall oxidation reaction may be formulated as shown below, where several reaction steps are required for the production of the intermediate symbolized as X.

Table 7

UNCORRECTED CHEMILUMINESCENCE AND FLUORESCENCE SPECTRA* OF INDOLES

Indole Derivative	Chemiluminescence Peak, nm	Fluorescence Peak in Neutral Solution, nm	Fluorescence Peak in Degassed Basic Solution, nm	Fluorescence Peak of Oxidized Solution, nm	Remarks
Indole	491	357 (350 in water, 330 in EtOH)[1]	394	400 394 400 393 396	2 cc of air injected into solution 7 cc of air injected into solution 12 cc of air injected int solution 17 cc of air injected into solution 22 cc of air injected into solution
5-Methylindole	523	336	407 413	406	15 minutes of O_2 flow at 0.04 cfm 60 minutes of O_2 flow at 0.04 cfm
7-Methylindole	432	374	386	384	15 minutes of O_2 flow at 0.04 cfm
3-Methylindole (skatole zone refined)	489	356 (370 in water, 350 in EtOH)[1]	430	430, 475 420, 480 420, 485	Initial stage of oxidation 3 minutes of O_2 flow 7 minutes of O_2 flow (reported in Tech Report No. 4)
3-Ethylindole	493	360	427	437	Oxygen flow for 20 minutes
L Tryptophan	[illegible]	370 (345,360 in H_2O)[1]	430	432	Oxygen flow for 20 minutes
2,5-Dimethylindole	492	370	406	409 424	6 minutes of O_2 flow at 0.025 cfm 25 minutes of O_2 flow
2,3-Dimethylindole in DMF	516	369 (364 shoulder) (376 in water, 360 in EtOH)[1]	423	- 514	DMF solution, 1×10^{-3}M indole, 0.1M base, recrystallized. Oxidation proceeded until solution was no longer chemiluminescent.

[1] B. L. Van Duuren, Chem. Rev., 63, 329 (1963).

* 3130, 3341 Å Excitation wavelengths

Table 7 (Continued)

Indole Derivative	Chemiluminescence Peak, nm	Fluorescence Peak in Neutral Solution, nm	Fluorescence Peak in Degassed Basic Solution, nm	Fluorescence Peak of Oxidized Solution, nm	Remarks
2,3-Dimethylindole	514	370 (362 shoulder)	423	427, 506	Indole was oxidized until chemiluminescence emission was negligible. Data previously reported in Technical Report No. 4.
Indole-5-carboxylic acid	514	376	414	-	Technical Report No. 4
Indole-3-acetic acid	-	352 (370 shoulder)	434	-	
Indole-3-acetic acid in DMF	490	353 (370 shoulder)	374	-	DMF solution.
5,6-Dibenzyloxyindole	516	-	-	-	Solution turned yellow while the fluorescence spectra were being taken.

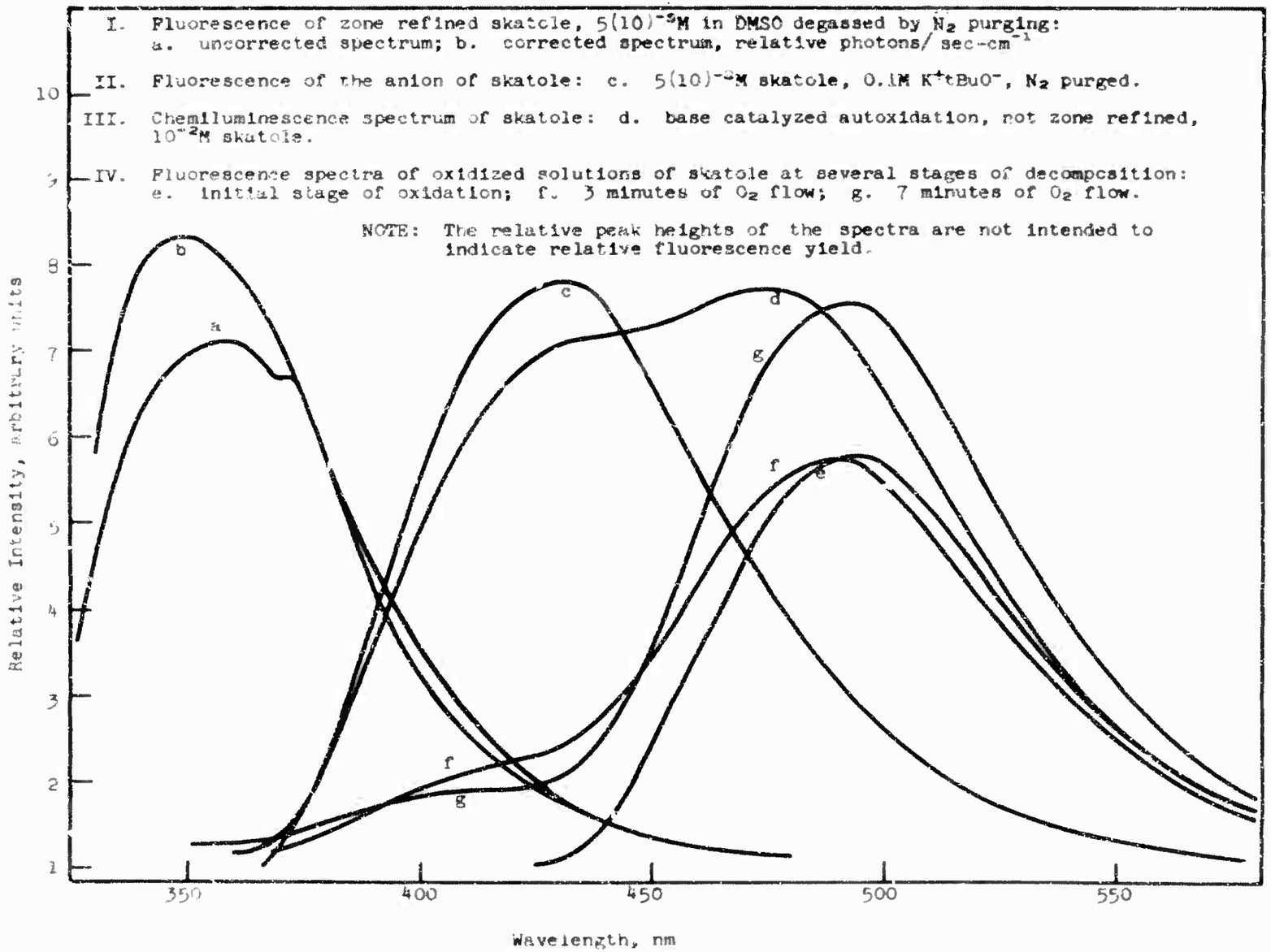
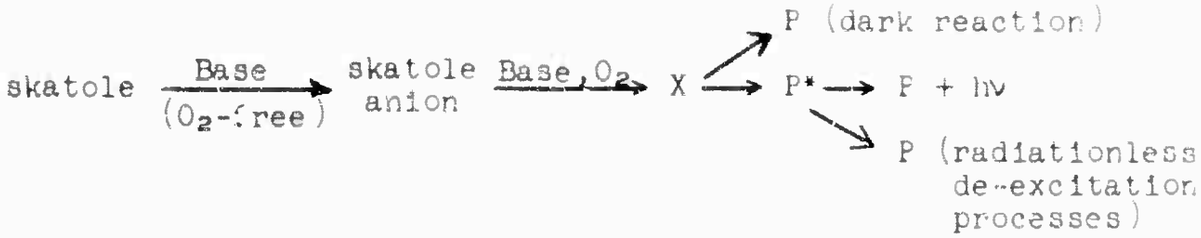


Figure 4. Chemiluminescence Spectrum of Skatole and Fluorescence Spectra of Skatole and its Oxidation Products



The fluorescence emission spectra of several possible oxidation products of the indoles have been obtained in an attempt to identify the emitting species. The observed emission peaks are given in Table 8. One of the products isolated from the aqueous persulfate oxidation of indole was anthranilic acid (ref. 11). The fluorescence of the anion of anthranilic acid in DMSO-0.1M t-butoxide peaks at a wavelength 20 nm to the blue of the indole chemiluminescence. The fluorescence spectrum of the oxidized solution does not reveal the 471 nm band characteristic of this anion, ruling out this species.

The peracetic acid-hydrogen peroxide oxidation of skatole and tryptophan yields as reaction products 3-methyloxindole and 3-oxytryptophan, respectively (ref. 12). The fluorescence peak for oxindole anion is, however found approximately 100 nm to the blue relative to the chemiluminescence peak of indole.

The oxidative ring cleavage product of skatole is ortho formamido acetophenone (see following section). We have determined the fluorescence spectrum of the related compound, ortho amino acetophone. Both neutral and basic solutions of this compound peak at 454 nm. In the basic solution a shoulder appears at approximately 510 nm. At present, it is not clear whether or not this spectrum is produced by the original species. The fluorescence spectra of the anion will be obtained as a function of concentration to resolve the problem and that of its formyl derivative.

A possible oxidation product of 2-methylindole is N-acetyl anthranilic acid. However, the peak of the fluorescence spectrum of the anion of this acid is at 448 nm or to the short wavelength side of all the chemiluminescence spectra of the indoles.

The oxidative ring cleavage product of 2,3-dimethylindole is orthoacetamidoacetophenone. We find that the fluorescence of the basic solution of this compound in DMSO peaks at a wavelength of 516 nm. There is excellent agreement between the contour of the fluorescence peak and the chemiluminescence emission from 2,3-dimethylindole (Figure 5). The inference, of course, is that the chemiluminescence results from the formation of the acetophenone product in the excited state.

Table 8

FLUORESCENCE SPECTRA OF POSSIBLE INDOLE OXIDATION PRODUCTS

Compound	Fluorescence* Peak, nm	Remarks
Anthranilic acid	411	10^{-3}M acid, 2540 Å, 3130 Å, 3314 Å, excitation
Anion of Anthranilic acid	471	5 x 10^{-3}M acid, 0.1M base, air-saturated solution
Anion of N-acetyl anthranilic acid	448	5 x 10^{-3}M acid, 0.1M base
Anion of Oxindole	384	5 x 10^{-3}M oxindole, 0.1M base
Ortho amino acetophenone	454	0.1M
Anion of ortho amino acetophenone	454; 510 (shoulder)	0.033M compound, 0.13M base, N_2 purged solution
Oxidized 2,3-Dimethylindole	506	5 x 10^{-3}M, 0.1M base + O_2
Ortho acetamido acetophenone	375; 510 (shoulder)	0.1M
Anion of Ortho acetamido acetophenone	516	0.13M base, 0.033M ortho acetamido acetophenone

* The 3130 and 3331 lines of low pressure mercury lamp were the exciting wavelength unless otherwise stated. Uncorrected spectra.

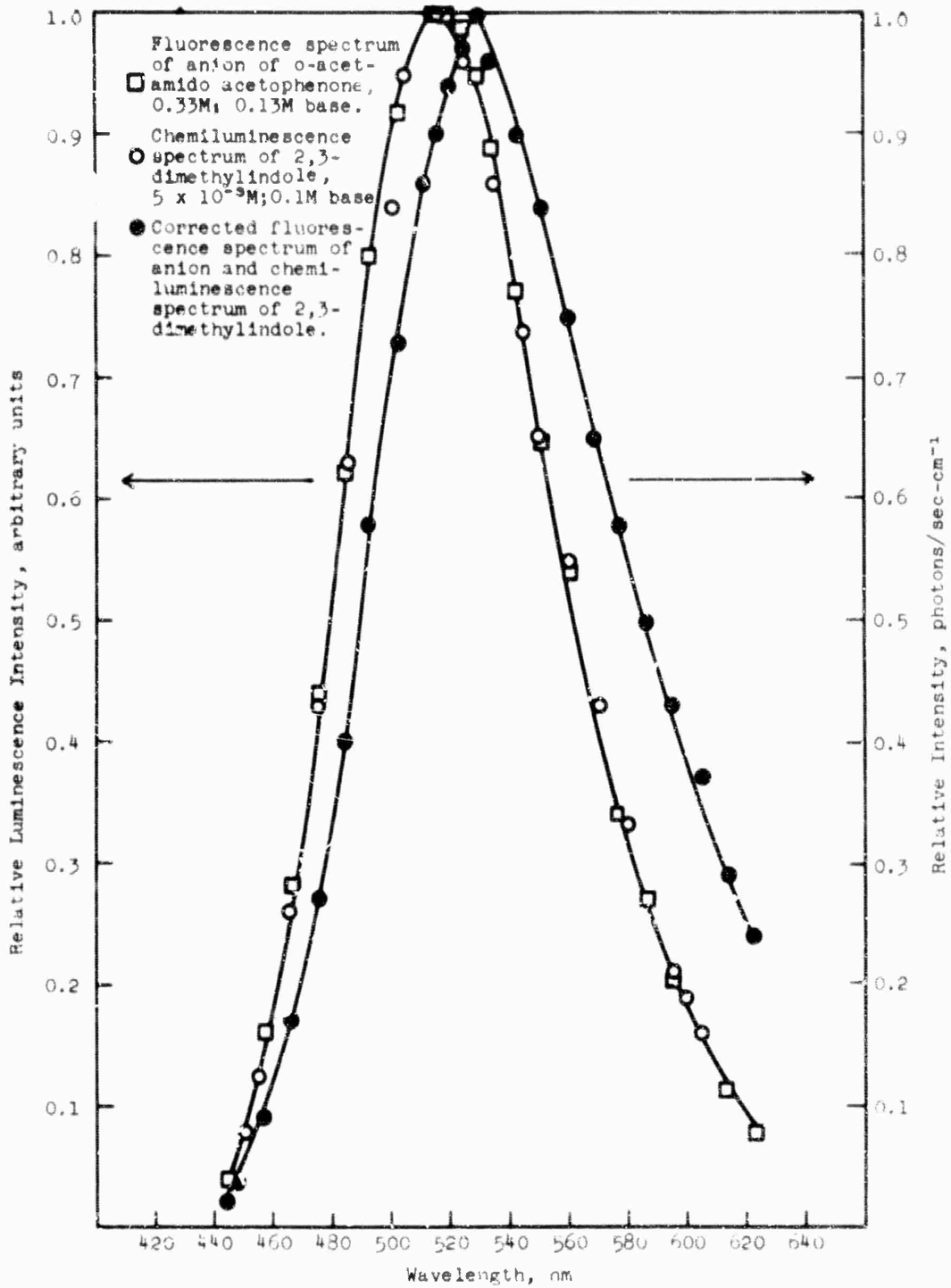


Figure 5. Comparison of the Fluorescence Spectrum of the Anion of o-Acetamido acetophenone to the Chemiluminescence Spectrum of 2,3-Dimethylindol

It is of interest to note that 3-ethylindole, unlike skatole, does not show a stable oxidation product fluorescence. However, for reasons which are not known, the skatole product fluorescence was not noted until the oxidation was repeated with the zone-refined material.

D. CHEMILUMINESCENCE DECAY KINETICS

We have examined in a preliminary way the kinetics of some chemiluminescence decays as determined from gross brightness photometer tracings. In general, the recordings do not exceed one half-life in duration and any conclusions drawn must be taken as tentative since it is recognized that unless apparent reaction order is maintained over several half-lives trivial fluctuations can easily lead to improper identification.

Random selection and analysis of a dozen decay curves gave the results shown in Table 9. The decay is found to be linear in three examples, exponential in six, and corresponds to no simple analytical function in the remaining three. The skatole results are of particular interest since they would imply a change of reaction order with concentration if confirmed. This result is not at all surprising for the postulated consecutive and parallel reactions that must occur in the indole oxidation (ref. 13).

The peak emission decay (initial) half-lives listed in the last column are derived from the fitted functions and are, therefore, more reliable averages than the values given in tables of chemiluminescence parameters. They are, however, generally smaller values than the "experimental" results. In part this results from the fact that the "kinetic" times are true decays from established steady state concentrations by the nature of the fitting process; that is, simple exponential decay does not occur from the observed peak of the brightness curve.

Figures 6 and 7 give examples of the exponential and linear decay curves observed. The plotted points are evenly spaced values read off the photometer tracings.

Table 9

DECAY KINETICS OF INDOLE CHEMILUMINESCENCE

Compound	Conc., molar	Run No.	Decay Function	Rate Constant	$t_{1/2}$, seconds
Indole-3-acetic acid	5×10^{-3}	6-21-4	$I = I_0e^{-kt}$	2.9×10^{-3}	240
L-Tryptophan	5×10^{-3}	5-26-1,2	$I = I_0e^{-kt}$	$(1.8\pm0.02)10^{-3}sec^{-1}$,	443±4
2,7-Dimethylindole	5×10^{-3}	7-22-1,2	$I = I_0e^{-kt}$	$(1.83\pm0.07)10^{-2}sec^{-1}$,	38±1
3-Ethylindole	5×10^{-3}	8-4-1,2	$I = I_0e^{-kt}$	$(1.66\pm0.9)10^{-3}sec^{-1}$,	417±22
3-Methylindole	6.6×10^{-2}	3-5-5	$I = I_0e^{-kt}$	$2.9 \times 10^{-3}sec^{-1}$	240
3-Methylindole	2×10^{-2}	3-5-1	$I = I_0e^{-kt}$	$2.0 \times 10^{-3}sec^{-1}$	342
3-Methylindole	10^{-2}	3-5-2	indeterminate	-	-
3-Methylindole	2.2×10^{-3}	3-3	$I = -I_0kt$	1.1×10^{-2} amp/sec	340
2,3-Dimethylindole	5×10^{-3}	4-30	$I = -I_0kt$	5.1×10^{-2} amp/sec	80
2,3-Dimethylindole in DMF	1.85×10^{-3}	7-15-2	$I = -I_0kt$	1.05×10^{-1} amp/sec	58
5-Benzyloxy-indole-3-acetic acid	5×10^{-3}	7-27	indeterminate	-	-
2,3,7-Trimethyl-indole	5×10^{-3}	6-18-1,2,3	indeterminate	-	-

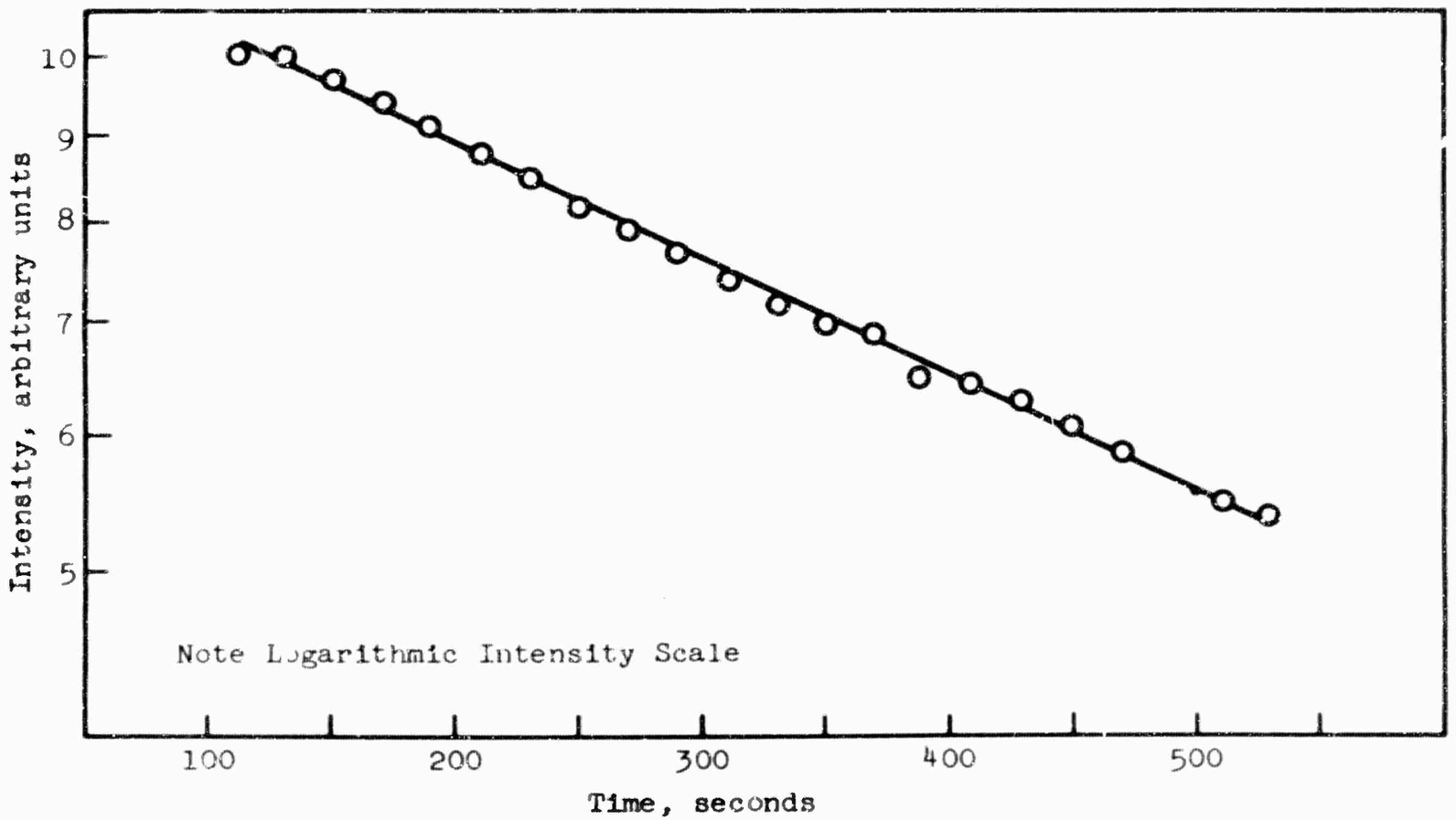


Figure 6. Kinetic Plot of the Chemiluminescence Decay Curve of 3-Ethylindole

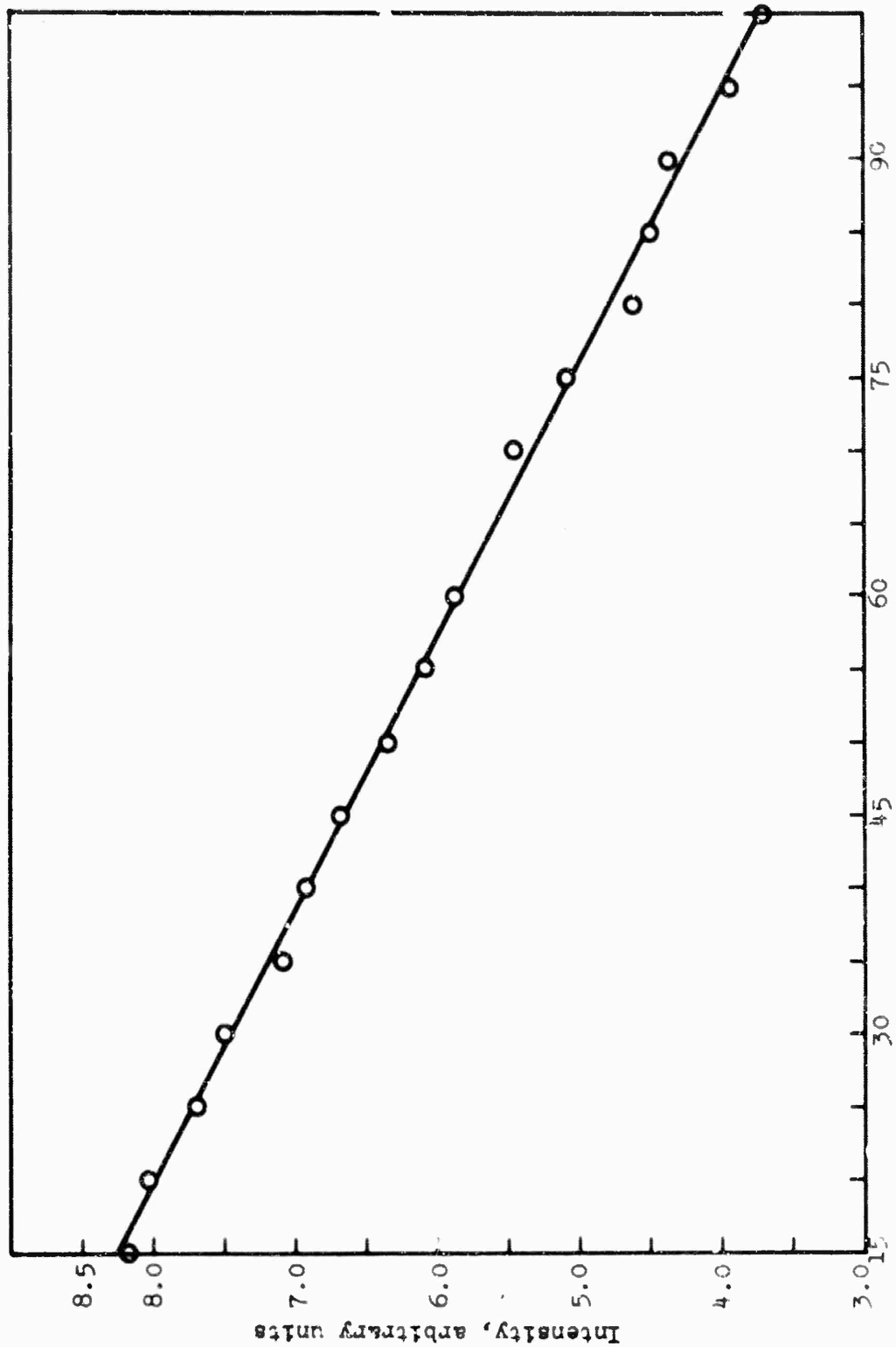


Figure 7. Kinetic Plot of the Chemiluminescence Decay Curve of 2,3-Dimethylindole

IV. HETEROGENEOUS CATALYSIS

A. INTRODUCTION

Several preliminary experiments have been performed to initiate the investigation of heterogeneous catalysis in chemiluminescent reactions.

B. EXPERIMENTAL

A simple, qualitative procedure was used to measure chemiluminescence emission resulting from the oxidation of luminol and lucigenin catalyzed by silica gel G. Sheets of silica gel were prepared by coating the gel on glass slides. The slides were dipped in a water-silica gel slurry and were air-dried at room temperature. Methanol solution of the organic compound was sprayed from an atomizer onto the silica gel and dried. The base and oxidant, if any, were sprayed independently on the dry slides.

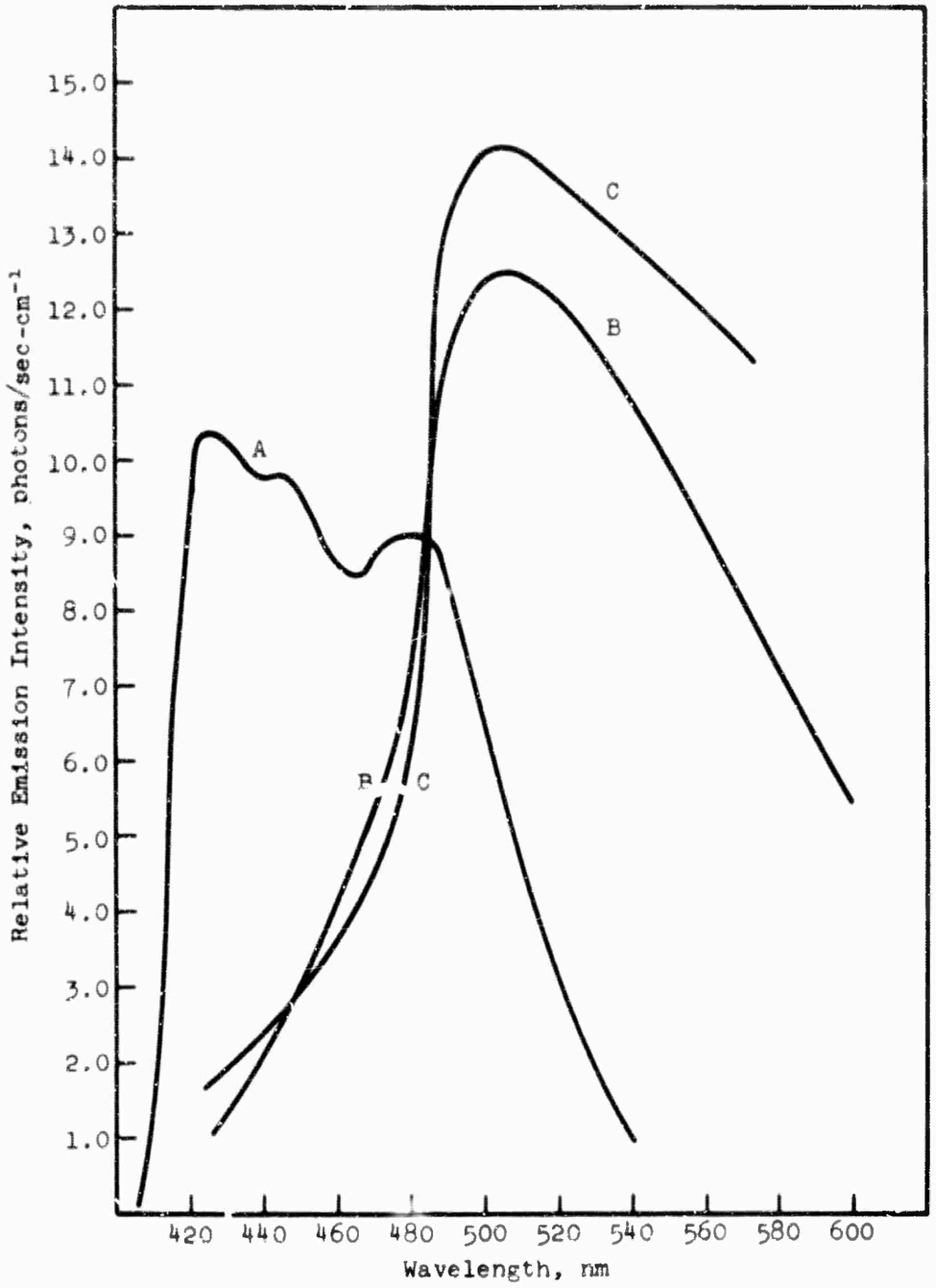
The chemiluminescence of the base catalyzed peroxidation of lucigenin was observed (Table 10). The blue-green emission appeared upon spraying of the final reaction component. The silica gel was wet during the course of the chemiluminescence, permitting the components (except for the solid substrate) to diffuse toward each other in the liquid phase. The decay of the light intensity was measured photometrically. The time required for the intensity to diminish to one half of its value was on the order of three minutes. The decay does not obey simple first order, second order or nonintegral order kinetics.

The chemiluminescence spectrum of the lucigenin oxidation in homogeneous ethanol solution is a broad, structured band between 420 nm and 490 nm (Figure 8). The emission from silica gel is shifted to the red, giving a broad band peaking at 505 nm. Similar emission spectra are obtained with either ammonia or sodium hydroxide. The oxidation of luminol by potassium tertiary butoxide and oxygen does not lead to chemiluminescence in the system investigated. This quenching of chemiluminescence upon adsorption on silica has also been observed for the indoles. Quenching of the fluorescence of the parent compound upon absorption also occurs. This is, presumably, the key factor in the quenching of the chemiluminescence.

Table 10

CHEMILUMINESCENT REACTION ON SILICA GEL ADSORBENT

Organic Compound	Base	Oxidant	Observation
Lucigenin	2M NaOH	10% H_2O_2 in ethanol	blue-green chemiluminescence
Lucigenin	4M NaOH	10% H_2O_2 in ethanol	decayed to one half peak intensity in 210 seconds
Luminol	0.05 to 0.1M K^+tBuO^-, DMSO solution	O_2	no chemiluminescence



A = 10^{-3}M Lucigenin, 4% H_2O_2, 6.8M NH_4OH in Ethanol

B = Lucigenin, 2M NaOH, 30% H_2O_2 absorbed on Silica Gel G

C = Lucigenin, conc. NH_4OH, 30% H_2O_2 absorbed on Silica Gel G

Figure 8. Chemiluminescence Spectra of Lucigenin in Ethanol Solution and on Silica Gel

V. INSTRUMENTATION

A. INTRODUCTION

The determination of the absolute fluorescence spectra, quantum yields, and brightness of chemiluminescent reactions requires calibration of the spectral sensitivity of the spectrometer. We have performed a relative calibration of the spectral sensitivity of our spectrometer in the near ultraviolet and visible spectrum by comparison to fluorescence standards.

B. EXPERIMENTAL

The fluorescence standards were selected from the literature (ref. 14, 15) to cover the spectral range between 320 nm and 660 nm. A low-pressure mercury lamp was used as the excitation source, oriented at a 90° angle relative to the spectrometer.

The conditions under which the fluorescence standards were used is given below:

(1) 5.0×10^{-4}M Naphthalene in ethanol; M.C.B., recrystallized from ethanol, mp 79-80°C; spectral range 324 to 370 nm (ref. 14); 254 nm excitation.

(2) 4.3×10^{-6}M Anthracene in ethanol; Eastman Kodak blue-violet fluorescent grade, used without further purification, spectral range 370 to 400 nm (ref. 14); 254 nm excitation.

(3) 1×10^{-4}M Quinine Sulfate in 1N sulfuric acid; M.C.B., mp 229°C; (The sulfate was used without further purification.) spectral range 400 to 500 nm (ref. 15); 3130 and 3330 Å excitation*.

(4) 1×10^{-4}M N,N-Dimethyl-m-nitroaniline in 30% by volume fluorescent grade benzene and 70% by volume of M.C.B. spectrograde heptane**, spectral range 500 to 660 nm (ref. 15); 3130 nm and 3330 nm excitation.

The emission spectrometer is a Mod 1700 Spex Czerny-Turner scanning spectrometer, equipped with a 1200-groove/mm grating

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* The literature mp is 235.2°C. The lower melting point is attributed to the presence of water of recrystallization, c.f. mp of quinine sulfate $\cdot 2H_2O$ is 205°C.

** M.C.B. spectrograde hexane contained some trace amount of fluorescent material and was not used. Lippert reports the spectrum in this solvent but the spectrum will be similar in heptane.

blazed at 5000 Å, and an E.M.I. 9558Q photomultiplier. The emitters are chosen so that the wavelength of each spectrum is overlapped by the adjacent spectra, permitting a continuous relative spectral sensitivity calibration. The sensitivity of the instrument is obtained by taking the ratio of the observed photocurrent, measured in microamperes, at a given wavelength and bandwidth, to the true relative spectral distribution of the emitter in units of photons/unit frequency interval. To obtain the relative sensitivity, the ratio at 376 nm was defined as unity. The sensitivities at the wavelengths where the anthracene intensity crosses naphthalene and quinine sulfate were calculated, and the relative sensitivity continued as a smooth function through the wavelengths of these emitters.

The relative sensitivity function obtained is shown in Figure 9. The curve is characterized by two maxima, at 376 nm and at 441 nm. The spectral range covered by each compound is designated in the legend.

The wavelength of the exciting source was chosen as to be near the maximum of the absorption band. This selection should reduce the effect of traces of fluorescent impurities. The concentrations were chosen to minimize the effects of self absorption. The gross features of the sensitivity function resembles the reported quantum efficiency curve of the photomultiplier in the blue and that reported by Parker for a similar system (ref. 16).

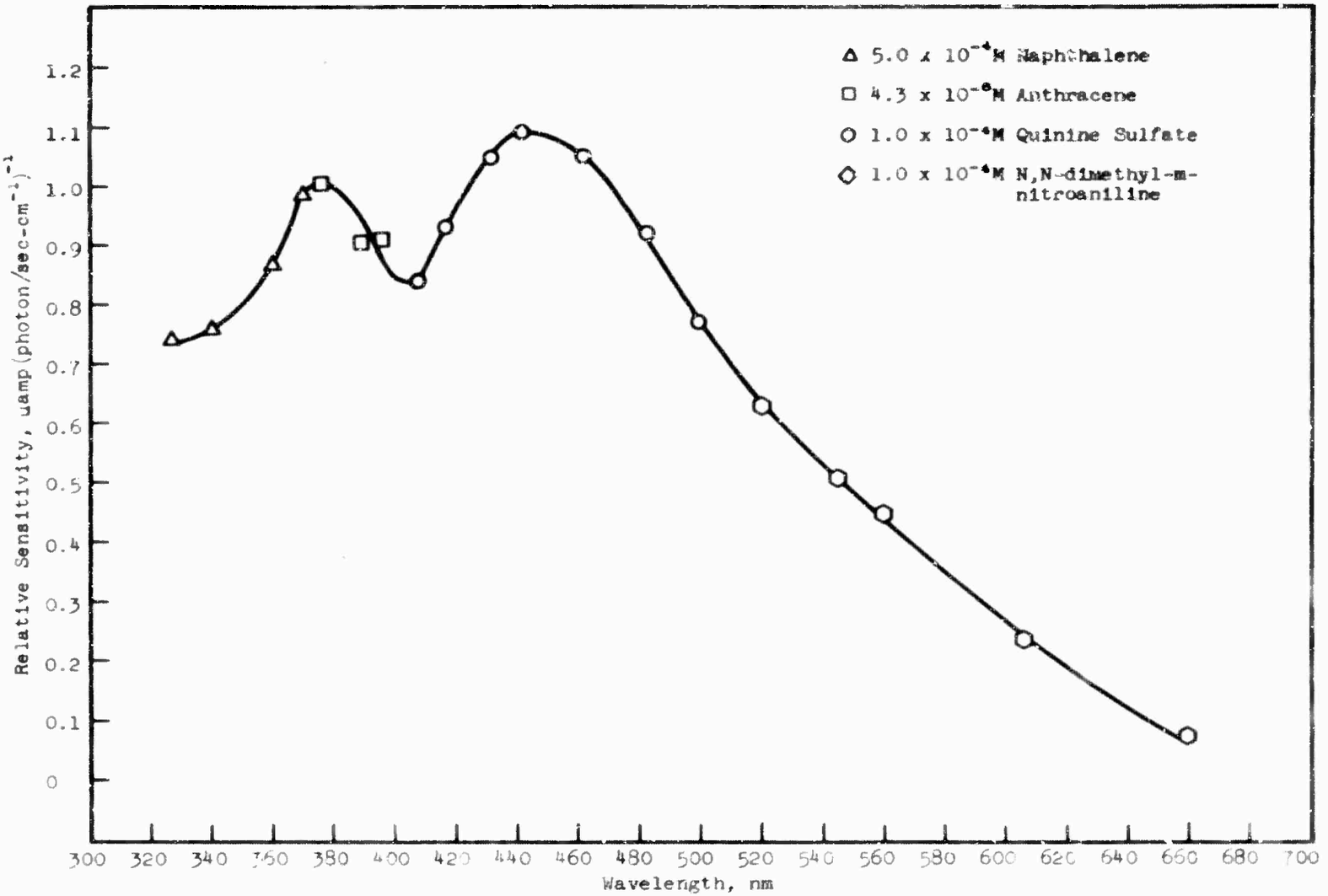

Figure 9. Relative Sensitivity of Spectrometer vs Wavelength

VI. FUTURE WORK

Synthesis of a number of probable intermediates in the oxidation of 3-methyl and 2,3-dimethylindoles will be carried out, and the properties of these compounds investigated. The hydroperoxides and other reactive intermediates will be examined as possible candidates for chemiluminescent reactants of high brightness and efficiency.

Synthesis of 3-methylindole-5-carboxylic acid, and possibly other 5,6-substituted indoles, will be undertaken in the continuing effort to obtain highly efficient chemiluminescence compounds. Research on optimum conditions for chemiluminescence of the brighter indoles will be continued, with emphasis upon the effect of sensitizers, solvents, oxidants, and base strength.

The absolute calibration of the spectrometer will be carried out using Seliger's recent data for luminol as a secondary standard (ref. 4). The photometers will be provided with integrating circuits to permit total emission comparisons in an attempt to improve reproducibility of the efficiency measurements.

A cell for convenient measurement of chemiluminescence parameters in heterogeneous reaction has been designed. The catalyst is incorporated in a porous Teflon membrane, permitting relatively free access of oxygen to the catalyst-reactant solution interface. The emission can be observed through a window parallel to the membrane surface.

VII. REFERENCES

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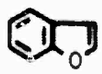
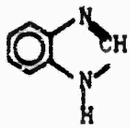
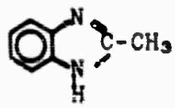
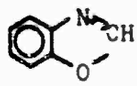
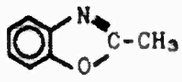
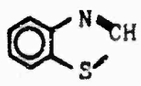
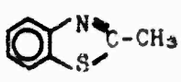
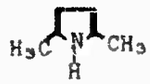
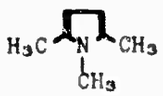
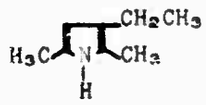
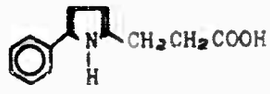
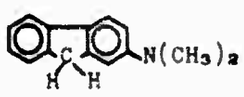
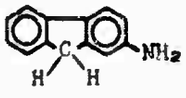
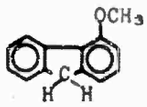
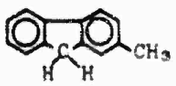
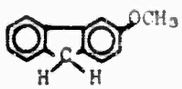
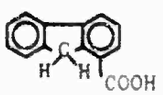
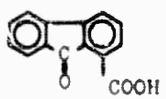
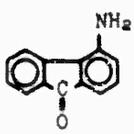
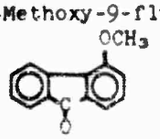
APPENDIX I

CHEMILUMINESCENCE OF MISCELLANEOUS COMPOUNDS

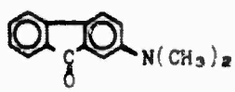
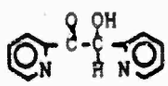
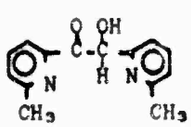
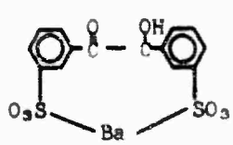
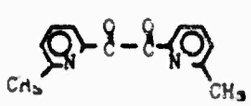
Compound and Structure	Peak O_2 Current Ratio I/I_0	Time to O_2 Peak sec	$T_{1/2}$ of O_2 Peak sec	Figure of Merit
a) Heterocyclic Analogues of Indene				
Benzofuran 	6×10^{-2}	15	35	2.1
Benzimidazole 	7.6×10^{-4}	30	120	9×10^{-2}
2-Methylbenzimidazole 	1.3×10^{-3}	18	72	9.4×10^{-2}
Benzoxazole 	6×10^{-3}	22	72	0.43
2-Methylbenzoxazole 	5×10^{-2}	30	42	0.2
Benzothiazole 	$(2.6 \pm 0.6) 10^{-3}$	15	45 ± 15	0.11
2-Methyl-Benzothiazole 	2×10^{-3}	12	12	24×10^{-3}

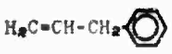
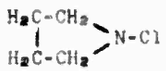
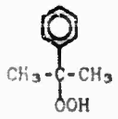
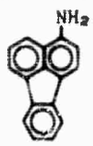
Compound and Structure	Peak O_2 Current Ratio I/I_o	Time to O_2 Peak sec	$T_{1/2}$ of O_2 Peak sec	Figure of Merit
	b) Pyrrole Derivatives			
2,5-Dimethylpyrrole 	1.2×10^{-2}	6	52	0.62
N-Methylpyrrole 	8×10^{-3}	15	20	0.16
1,2,5-Trimethylpyrrole 	. $^{-3}$	10	45	4.5×10^{-2}
2,4-Dimethyl-3-ethyl Pyrrole 	3.2×10^{-3}	60	90	0.29
5-Phenyl-2-pyrrole Propionic acid 	1.6×10^{-2}	8	9	0.14
	c) Fluorene and Fluorenone Derivatives			
2-Dimethylamino fluorene 	$(2.2 \pm 0.7)10^{-2}$	32	5 ± 1	0.11
2-Amino fluorene 	1.9×10^{-2}	26	11	0.21

APPENDIX I (Continued)

Compound and Structure	Peak O_2 Current Ratio I/I_o	Time to O_2 Peak sec	$T_{1/2}$ of O_2 Peak sec	Figure of Merit
4-Methoxyfluorene 	$(2.5 \pm 0.3)\ 10^{-2}$	17	66 ± 54	1.8
2-Methylfluorene 	8.4×10^{-2}	30	10	0.84
3-Methoxyfluorene 	0.4 ± 0.15	26 ± 10	10 ± 7	4.2 ± 3.6
1-Fluorene-carboxylic Acid 	6×10^{-2}	24	30	1.8
9-Fluorenone-1-carboxylic Acid 	3.4×10^{-2}	6	132	4.5
4-Amino-9-Fluorenone 	1.1×10^{-3}	12	24	26×10^{-3}
4-Methoxy-9-fluorenone 	2.2×10^{-3}	24	54	0.119

APPENDIX I (Continued)

Compound and Structure	Peak O_2 Current Ratio I/I_0	Time to O_2 Peak sec	$T_{1/2}$ of O_2 Peak sec	Figure of Merit
2-Dimethylamino-9-fluorenone 	2.2×10^{-2}	17	24	0.53
d) Acyloins and 1,2-diketones				
α-Pyridoin 	$(2.3 \pm 0.3)10^{-2}$	31 ± 17	3 ± 1	$(6.4 \pm 1.2)10^{-2}$
6,6'-Dimethyl-2,2'-pyridoin 	3.5×10^{-2}	40	2	7×10^{-2}
Barium Benzoin-3,3'-Disulfonate 	$\approx 0.6 \times 10^{-3}$	<5	≈10	$\approx 6 \times 10^{-3}$
2,2'-Pyridyl 	1.4×10^{-2}	12	3	4.2×10^{-2}
6,6'-Dimethyl-2,2'-pyridyl 	1.2×10^{-3}	6	3	3.6×10^{-3}

Compound and Structure	Peak O_2 Current Ratio I/I_0	Time to O_2 Peak sec	$T_{1/2}$ of O_2 Peak sec	Figure of Merit
e) Compounds Containing an Olefinic Linkage				
Sorbic Acid $CH_3CH{=}CH{-}CH{=}CH{-}COOH$	1.8×10^{-3}	10	20	39×10^{-3}
Tetracyanoethylene 	4.8×10^{-3}	5	10	48×10^{-3}
Allyl benzene 	1.7×10^{-3}	~10	~30	5.1×10^{-3}
Tetracyanoquinodimethane (TCNQ) 	2×10^{-4}	<5	--	--
f) Miscellaneous				
N-chlorosuccinimide 	1×10^{-3}	25	120	.120
Cumene Hydroperoxide 	5.4×10^{-3}	10	10	54×10^{-3}
Acenaphthene 	1.4×10^{-3}	17	60	8.4×10^{-2}
3-Aminofluoranthene 	9.2×10^{-3}	190	84	0.77

APPENDIX II

ORGANIC SYNTHESIS

1. 2,3-Dimethylindole-5-carboxylic Acid

This indole was prepared in 30% overall yield (three steps) according to the procedure of Verkade and Lieste (ref. 17).

a. 2-(p-Carbethoxyphenyl)amino-3-butanone (I)

Alkylation of ethyl p-aminobenzoate with 3-bromo-2-butanone in aqueous alcohol with sodium bicarbonate as an acid scavenger provided I as a tan solid (46%) after charcoaling and recrystallization from diethyl ether-petroleum ether (bp 30-60°C); mp 72.5-73.5°C.

b. Ethyl 2,3-Dimethylindole-5-carboxylate (II)

Reaction of I with the hydrochloride salt of ethyl p-aminobenzoate (prepared by treatment of the amino ester with anhydrous hydrogen chloride in absolute ethanol-diethyl ether; mp 206-208°C) yielded II as a light tan solid (70%) with mp 109-111°C. Recrystallization from diethyl ether-petroleum ether (bp 30-60°C) raised the mp to 114-115.5°C. No impurities were detected by VPC and NMR analysis.

c. 2,3-Dimethyl-5-carboxylic Acid

Saponification of II with alcoholic potassium hydroxide, followed by acidification, provided the acid as a tan solid in 93% yield with mp 237-239°C. Charcoaling and recrystallization did not substantially change the mp (mp 238-239.5°C).

2. 3-Ethylindole

This compound was prepared in 66% yield by the lithium aluminum hydride reduction of 3-acetylindole according to the procedure of Leete and Marion (ref. 18). The crude product was purified by distillation (bp 83-84°C/13-14 mm); the distillate solidified in the receiver to an off-white solid (mp 33-34°C; reported (ref. 19) 42°C, (ref. 19) 33-35°C). The infrared spectrum was consistent with the structure.

3. O-Acetamidoacetophenone

o-Acetamidoacetophenone, mp 72-74°C (lit. mp 74-75°C) was prepared in 80% yield by the method of Leonard and Boyd (ref. 20). The formylation of o-aminoacetophenone is being attempted by means of a mixed anhydride acylation reaction (ref. 21).

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MONSANTO RESEARCH CORPORATION
BOSTON LABORATORY
Everett, Massachusetts 02149

ERRATA

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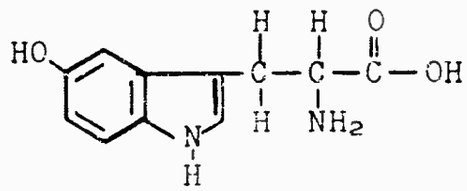
Report Period: 1 June - 31 August 1965
Contract No: Nonr-4511(00)
ARPA Order No. 299
Task 356-464
Report Date: 30 September 1965

Please make corrections as noted below:

Page 1, para. 4, l. 6: delete "peak"

Page 5, line 3, column 4: $T_{1/2}$ is $(6.4 \pm 1.4)10^3$

Page 9, line 1: formula for 5-hydroxytryptophan should be



Page 19, line 1, column 5: $t_{1/2}$ is 325, not 235.

Page 20, footnote: change 0.1% to 0.3%

Page 26: curve "d" should be labeled "e";
curve "e" should be labeled "d".

Page 31: lines 8, 9, 10, column 4: equations should read:

$$I = I_o - kt$$

not $I = -I_o kt$.